IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re continuation application of:			
Wayne GODFREY *et al.*		Art Unit:	Not yet assigned
Appln. No.:	Not yet assigned	Examiner:	Not yet assigned
Filed:	Herewith	Atty. Docket:	16524.010
For:	Receptor on the Surface of Activated T-Cells (ACT-4)		

Preliminary Amendment

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

Prior to examination on the merits, Applicants hereby request entry of the following amendments in the above-captioned application:

In the Specification:

Please delete the heading entitled "Attorney Docket No. 05490A-022000" on page 1.

Please **add** the following paragraphs on page 1 before the paragraph entitled "Technical Field":

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of co-pending U.S. Patent Application Serial No. 08/472,940 filed June 6, 1995, which is a divisional of U.S. Patent Application Serial No. 08/147,784, filed November 3, 1993, now U.S. Patent No. 5,821,332, both of which applications are herein incorporated by reference in their entirety.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

This invention was made with Government support under contract CA24607 awarded by the National Institutes of Health. The Government has certain rights in this invention.

INCORPORATION OF SEQUENCE LISTING

A paper copy of the Sequence Listing and a computer readable form of the sequence listing on diskette, containing the file named SeqList.txt, which is 6581 bytes in size (measured in MS-DOS), and which was created on April 17, 2001, and recorded on April 28, 2001, are herein incorporated by reference.

Please **delete** the paragraph beginning with the phrase "Fig. 5:" on page 6 **and replace** it with the following paragraph:

Fig 5: cDNA (upper) (SEQ ID NO: 1) and deduced amino acid sequence (lower) (SEQ ID NO:2) of ACT-4-h-1. The Figure indicates the locations of an N-terminal signal sequence, two possible signal cleavage sites (vertical arrows), two glycosylation sites (gly), a transmembrane domain (TM), a stop codon and a poly-A signal sequence.

Please **delete** the paragraph beginning with the phrase "All hybridomas" on page 30 **and replace** it with the following paragraph:

All hybridomas, triomas and other cell lines producing the antibodies and their fragments discussed, *supra*, are expressly included in the invention. These include the hybridoma line HBL106, deposited as ATCC Accession No. ATCC HB 11483, which produces the L106 mouse antibody.

Please **delete** the paragraph beginning with the phrase "Mice were immunized" and which spans from page 42, line 30 to page 43, line 2 and **replace it** with the following paragraph:

Mice were immunized with PHA-transformed T-lymphoblasts. Splenocytes from immunized mice were fused with SP2/O myeloma cells and hybridomas secreting antibodies specific for the T-cell clone were selected. The hybridomas were cloned by limiting dilution. A monoclonal antibody, designated L106, produced by one of the resulting hybridoma, was selected for further characterization. The L106 antibody was found to have an IgG1 isotype. A hybridoma producing the antibody, designated HBL106 has been deposited at the American

Type Culture Collection, now located at 10801 University Boulevard, Manassas, Virginia 20110-2209, on 3 November 1993, and assigned ATCC Accession No. ATCC HB 11483.

On page 60, please **delete** the footer entitled "5490A220.APP" on the bottom of the page.

In the Claims:

Please cancel claims 1-25, 28-30, 32, 34, and 36-58 without disclaimer or prejudice to the underlying subject matter.

Please amend claims 26, 27 and 31 as follows:

26. (Amended) The antibody of claim 31 that inhibits activation of $CD4^+$ T-cells.

27. (Amended) The monoclonal antibody of claim 31 that stimulates activation of $CD4^+$ T-cells.

31. (Amended) A monoclonal antibody that is L106.

Please add new claims 59-77 as follows:

59. A monoclonal antibody that specifically binds to an ACT-4-h-1 receptor polypeptide and is generated by hybridoma HBL106, deposited under ATCC Accession No. HB11483.

60. A fragment of an L106 antibody that specifically binds to an ACT-4-h-1 receptor polypeptide with a binding affinity of at least 10^7 M.

61. The fragment of claim 60, wherein said fragment is selected from the group consisting of a heavy chain, a light chain, a Fab fragment, a Fab' fragment, a $F(ab')_2$ fragment, a Fabc fragment, and a Fv fragment.

62. A monoclonal antibody produced by hybridoma HBL106, deposited under ATCC Accession No. HB11483.

63. A cell of hybridoma HBL106, deposited under ATCC Accession No. HB11483.

64. A humanized antibody comprising a humanized heavy chain, wherein the humanized heavy chain comprises three complementarity determining regions corresponding to the complementarity determining regions of an L106 antibody heavy chain.

65. The humanized antibody of claim 64, wherein said humanized antibody specifically binds to an ACT-4-h-1 receptor polypeptide with a binding affinity that is within three-fold of the binding affinity of an L106 antibody.

66. A fragment of the humanized antibody of claim 64, wherein said fragment specifically binds to an ACT-4-h-1 receptor polypeptide.

67. A humanized antibody comprising a humanized light chain, wherein the humanized light chain comprises three complementarity determining regions corresponding to the complementarity determining regions of an L106 antibody light chain.

68. The humanized antibody of claim 67, wherein said humanized antibody specifically binds to an ACT-4-h-1 receptor polypeptide with a binding affinity that is within three-fold of the binding affinity of an L106 antibody.

69. A fragment of the humanized antibody of claim 67, wherein said fragment specifically binds to an ACT-4-h-1 receptor polypeptide.

70. A humanized antibody comprising (a) a humanized light chain, wherein the humanized light chain comprises three complementarity determining regions corresponding to the complementarity determining regions of an L106 antibody light chain, and (b) a humanized heavy chain, wherein the humanized heavy chain comprises three complementarity determining regions corresponding to the complementarity determining regions of an L106 antibody heavy chain.

71. The humanized antibody of claim 70, wherein said humanized antibody specifically binds to an ACT-4-h-1 receptor polypeptide with a binding affinity that is within three-fold of the binding affinity of an L106 antibody.

72. A fragment of the humanized antibody of claim 70, wherein said fragment specifically binds to an ACT-4-h-1 receptor polypeptide.

73. A method of detecting activated $CD4^+$ T-cells in a sample, comprising:

contacting the sample and an L106 antibody; and

detecting specific binding between the sample and the L106 antibody to reveal the presence of activated $CD4^+$ T-cells in the sample.

74. The method of 73, wherein said method is a method of detecting activated $CD4^+$ T-cells in a tissue sample.

75. The method of 73, wherein said method is a method of detecting activated $CD4^+$ T-cells in a blood sample.

76. A method of detecting activated $CD4^+$ T-cells in a patient, comprising:

administering a diagnostic reagent comprising L106 antibody to a patient; and

detecting specific binding between cells of the patient and the L106 antibody, wherein the detection of specific binding is indicative of the presence of activated $CD4^+$ T-cells in the patient.

77. The method of 76, wherein the presence of activated $CD4^+$ T-cells is diagnostic of a disease or condition of the immune system.

Remarks

Claims 1-25, 28-30, 32, 34, and 36-58 have been cancelled, claims 26, 27 and 31 have been amended, and new claims 59-77 have been added. Support for new claims 59-77 may be found in the specification, for example at page 23, line 31 through page 30, line 22, and page 34, line 28 through page 36, line 15, and in the original claims. No new matter enters by this amendment. The application presently contains claims 26, 27, 31, 33, 35, and 59-77. The Sequence Listing has been formatted to comply with current 37 C.F.R. § 1.821 et seq., and a typographical error (the total number of bases in SEQ ID NO: 1) has been corrected. No new matter enters by this amendment.

The specification has been amended to update cross-reference to related application information, and to specify that the present application is a continuation application of co-pending application 08/472,940. The specification has also been amended to provide the references to the Sequence Listing which were made in the parent application No. 08/472,940 by the Examiner's Amendment of February 9, 2001. No new matter enters by this amendment.

The presently pending claims are believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. The Examiner is respectfully requested to contact Applicant's undersigned representative at 202.942.5071 to address any unresolved issues remaining in this application.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 50-1824.

Respectfully submitted,

David R. Marsh (Reg. No. 41,408)
June E. Cohan (Reg. No. 43,471)

Date: May 11, 2001

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Marked up versions

In the Specification:

On page 6:

Fig 5: cDNA (upper) **(SEQ ID NO: 1)** and deduced amino acid sequence (lower) **(SEQ ID NO:2)** of ACT-4-h-1. The Figure indicates the locations of an N-terminal signal sequence, two possible signal cleavage sites (vertical arrows), two glycosylation sites (gly), a transmembrane domain (TM), a stop codon and a poly-A signal sequence.

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On pages 42-43:

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In the Claims:

26. (Amended) The antibody of claim **31** [25] that inhibits activation of $CD4^+$ T-cells.

27. (Amended) The monoclonal antibody of claim **31** [25] that stimulates activation of $CD4^+$ T-cells.

31. (Amended) [The] **A monoclonal** antibody [of claim 29] that is L106.